NORTH-WEST UNIVERSITY
YUNIBESITI YA BOKONE-BOPHIRIMA
NOORDWES-UNIVERSITEIT

Cardiovascular function and psychological distress in urbanised black South Africans: The SABPA study

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Thesis submitted in fulfilment of the requirements for the degree Magister of Scientiae in Physiology

School for Physiology, Nutrition and Consumer Sciences
North-West University, Potchefstroom campus

March 2009

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THE ROAD NOT TAKEN

Two roads diverged in a yellow wood,
And sorry I could not travel both
And be one traveler, long I stood
And looked down one as far as I could
To where it bent in the undergrowth;

Then took the other, as just as fair,
And having perhaps the better claim,
Because it was grassy and wanted wear;
Though as for that the passing there
Had worn them really about the same,

And both that morning equally lay
In leaves no step had trodden black.
Oh, I kept the first for another day!
Yet knowing how way leads on to way,
I doubted if I should ever come back.

I shall be telling this with a sigh
Somewhere ages and ages hence:
Two roads diverged in a wood, and

I took the one less traveled by,
And that has made all the difference!

Robert Frost

ACKNOWLEDGEMENTS

The Author of this book would like to thank the following who without whom the completion of this dissertation would have not been possible:

- The Heavenly Father for all the blessing He has granted me throughout my studies.
- My mother and father for their love and support. Their dedication to my success has motivated and made me the person I am today.
- My supervisor, Professor J.M. Van Rooyen for the motivation and emotional and academic support.
- My co-supervisors: Professor L. Malan for the driving force and the motivation behind this study.
- Assistant supervisor: Dr. J. Potgieter, without whom the understanding of the psychological data would have been impossible.
- Contributors to the SABPA project: students, participants, data sampling, analysis and interpretation of data.
- My Brothers for their constant emotional support.
- Professor L.A. Greyvenstien for the language editing.
- The sponsors of the SABPA project: the North-West University: AUTHER (African Unit for Transdisiplinary Health Research); National Research Foundation (NRF); Medical Research Council (MRC). Metabolic Syndrome Institute (France).

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DECLARATION BY AUTHORS

The contribution of each of the researchers involved in this study is given in the following table:

Name	*Role in this study*
Me N Mashele (Physiologist)	Responsible for literature searches, statistical analyses, processing of data, design and planning of manuscript, interpretation of results and writing of the manuscript
Prof JM van Rooyen (Physiologist)	Supervisor. Supervised the writing of the manuscript, initial planning and design of manuscript, technical advice regarding literature, statistical analyses and interpretation of results.
Prof L Malan (Physiologist)	Co-supervisor. Supervised the writing of the manuscript, initial planning and design of manuscript, technical advice regarding literature, statistical analyses and interpretation of results.
Dr. JC Potgieter (Psychologist)	Co-supervisor. Supervised the writing of the manuscript, technical advice regarding literature, statistical analyses, and interpretation of results.

The following is a statement from the co-authors confirming their individual roles in the study and giving their permission that the article may form part of this dissertation.

I declare that I have approved the above-mentioned manuscript, that my role in the study, as indicated above, is representative of my actual contribution and that I hereby give consent that it may be published as part of the M.Sc. dissertation of Me N Mashele.

Prof. JM. van Rooyen Prof. L. Malan Dr. JC. Potgieter

AFRIKAANSE TITEL: Kardiovaskulêre funksie en psigologiese distres in verstedelikte swart Suid Afrikaners: Die SABPA studie

OPSOMMING

Motivering: Kardiovaskulêre siektes(KVS) is een van die vernaamste oorsake van wêreldwye sterftes, met die hoogste mortaliteitstempo in lande met lae en middel inkomste. Die verhoogde voorkoms van risiko faktore soos hipertensie, obesiteit en diabetes in Sub-Sahara Afrika, het verhoogde voorkoms van KVS tot gevolg. Dit is egter nog onduidelik of stres en meer spesifiek, die ervaring van psigologiese angs (distres), 'n bydrae lewer tot die verhoogde voorkoms van kardiovaskulêre siektes in hierdie populasie groep.

Volgens ons kennis is daar nog geen navorsing in 'n Afrika konteks gedoen oor die assosiasie tussen depressie, as 'n nagevolg van psigologiese angs, en kardiovaskulêre wanfunksie by Afrikane nie. Verdere navorsing op hierdie populasie groep kan dus as baanbrekerswerk beskou word.

Doel: Die doel van hierdie studie was om die assosiasie tussen psigologiese angs en kardiovaskulêre funksie in verstedelikte swart Suid-Afrikaners te ondersoek. Dit het 'n teiken populasie van 200 Afrikane, mans (n=101) en vrouens(n=99) ingesluit. Die deelnemers is ingedeel in 'n hipertensiewe (NT) groep.

Metadologie: Die manuskrip wat in Hoofstuk 2 voorgelê word, is afkomstig van die SABPA (Simpatiese aktiwiteit en Ambulatoriese Bloeddruk in Afrikane)projek. 'n Groep van 200 swart Afrikane is vanuit regeringsinstansie van die Noord-Wes Provinsie van Suid-Afrika, gewerf. Alle prosedures wat tydens die studie uitgevoer is, is deur die Noord-Wes Universiteit Etiek Komitee goedgekeur en die deelnemers het vooraf ingeligte toestemming gegee. Antropometriese metings is geneem met die bystand van 'n geregistreerde Biokinetikus. Rustende kardiovaskulêre, veranderlikes soos harttempo (HT), arteriële kompliansie (C_w), totale perifere weerstand (TPR) en gemiddelde arteriële druk (GAP) is geneem deur gebruik te maak van 'n Finometer apparaat. Die polsgolfsnelheid is verkry deur gebruik te maak van die Complior apparaat. Die 24 uur ambulatoriese bloeddruk (BD) metings is geneem deur gebruik te maak van 'n Cardiotens apparaat. Met behulp van die rustende EKG NORAV PL-1200 data is linker ventrikulêre hipertrofie gevind, deur gebruik te maak van die Cornell product ($RaVL + SV_3$) * QRS. Met behulp van gesondheidsvraelyste is die persepsie van gesondheid (General Health Questionnaire; GHQ-28) en die graad van depressie (Patient Health Questionnaire; PHQ-9) geassesseer. Die deelnemers is op grond van die "European Society of Hypertension (ESH)" 2007 se riglyne, in 'n hipertensiewe en normotensiewe groep verdeel, deur gebruik te maal van die 24 uur AMBP as 'n norm. Resultate verkry vanuit statistiese analises is aangepas vir uitskieters (ouderdom, liggaamsmassa indeks, alkohol inname en fisieke aktiwiteit). Statistiese analises is gedoen om die betekenisvolle verskille tussen ouderdom, liggaamsmassa indeks leefstyl, faktore en kardiovaskulêre veranderlikes en psigologiese parameters te bepaal. Die leser word na Hoofstuk 2 verwys, vir 'n meer

gedetailleerde beskrywing van die proefpersone, studie ontwerp en analitiese metodes gebruik.

Resultate en Gevolgtrekking: Die hipertensiewe (HPT) mans en vrouens was meer obees (p>0.01) met 'n groter middel omtrek (MO) (p=0.05) in vergelyking met hul normotensiewe(NT) teenvoeters. Die HPT groep (mans alleen) het ook 'n hoër Cornell produk waarde (p=0.06) opgelewer vergelyking met die normtensiewe groep. By die HPT mans daar 'n positiewe assosiasie ten opsigte van persepsie van fisieke gesondheid en bloeddruk (SBP en DBP), terwyl dit by die HPT vrouens geassosieer word met harttempo(HT). Erge depressie is geassosieer met linker ventrikulêre hipertrofie by HPT mans en met GAP by die HPT dames. Na 'n logistiese regressie analise om die verhouding tussen depressie en persepsie van gesondheid tot HPT te bepaal, is gevind dat depressie die grooste by bydraende faktor tot hipertensie in Afrikane is. Dit is aangetoon dat depressiewe vrouens se kans om hipertensie te ontwikkel 1.13 keer groter is as mans.

Hierdie resultate stel dus 'n moontlike assosiasie tussen depressie, as 'n uitkoms van psigologiese distres en kardiovaskulêre wanfunksie in verstedelikte Afrikane vaar en dat depressie 'n prominente bydrae lewer tot hipertensie in Afrika vroue.

Sleutelwoorde: depressie; persepsie van gesondheid; kardiovaskulêre funksie; verstedelikte Afrikane; hipertensie

TITLE: Cardiovascular function and Psychological distress in Urbanised black South Africans: the SABPA Study

SUMMARY

Motivation: Cardiovascular disease (CVD) is one of the leading causes of death worldwide, with the greatest mortality rates occurring in low and middle income countries. The increase in the prevalence of risk factors such as hypertension, obesity and diabetes in Sub-Saharan Africa has led in an increase of the prevalence of CVD. It remains largely unclear whether psychological distress and more specifically the perception of own health and / depression may contribute to this observed increase in the prevalence of CVD in this population group.

To our knowledge investigations exploring these aspects have not been done in the African context, thus the association between depression as an outcome of psychological distress and cardiovascular dysfunction in Africans is a new frontier that requires further exploration in the population group.

Objective: The aim of this study was to investigate the association between psychological distress and cardiovascular function in urbanized black South Africans which included a target population of 200 Africans, men (n=101) and women (n=99). The participants were stratified into a hypertensive (HT) and normotensive (NT) group.

Methodology: the manuscript presented in chapter 2 made use of the data obtained from the SABPA (Sympathetic activity and Ambulatory Blood Pressure in Africans) project. A group of 200 black Africans from governmental institutions of the North West Province

of South Africa were recruited. All procedures conducted were approved by the North-West University Ethics Committee and written informed consent was given by all the participants prior to the study. Anthropometric measurements were taken with the assistance of registered biokinetisists. Resting cardiovascular variables such as heart rate (HR), arterial compliance (C_w), total peripheral resistance (TPR) and the mean arterial pressure (MAP) were obtained with the use of a Finometer device. The 24 hours ambulatory blood pressure (BP) (AMBP) measurements were obtained with a Cardiotens apparatus. The resting ECG NORAV PL-1200 data determined left ventricular hypertrophy (LVH) by making use of the Cornell product ($RaVL + SV_3$) * QRS. Psychological distress questionnaire assessed the perception of health (General Health Questionnaire; GHQ-28) and depression severity (Patient Health Questionnaire; PHQ-9). Participants were stratified into hypertensive and normotensive groups based on the European Society of Hypertension (ESH) 2007 guidelines using the 24hr AMBP as a norm.

Results were adjusted for confounders (age, body mass index, smoking, alcohol consumption and physical activity). One way Analysis of Covariance (ANCOVA) was done to determine significant differences between age, body mass index, lifestyle factors cardiovascular variables and psychological parameters.

For more detailed description of the subjects, study design and analytical procedures used in this study the reader is referred to the Methods section in Chapter 2.

Results and Conclusion: The hypertensive (HT) men and women were more obese ($p<0.01$) with a larger waist circumference (WC) ($p=0.05$) and a lower compliance

($p \leq 0.05$) compared to their normotensive (NT) counterparts. Only the HT men revealed a higher Cornell product value ($p=0.06$) compared to NT counterparts. In HT men, somatisation was positively associated with blood pressure (SBP & DBP), while in HT women it was associated with heart rate (HR). Major depression was associated with a left ventricular hypertrophy in HT men and MAP in HT women. Logistic regression analysis followed to predict the strongest contributor to HT in Africans. It was indicated that depressed women are 1.13 times more likely to develop hypertension than men.

In conclusion, these results suggest a possible association between depression as an outcome of psychological distress and cardiovascular dysfunction in urbanised Africans. Depression has also been identified as a contributor to HT in African women.

Keywords: depression; perception of health; cardiovascular function; urbanized Africans; hypertension.

PREFACE

The structure and layout of this study is in manuscript format. The script is divided into three chapters: Chapter 1 serves as the foundation, background and motivation for this study. Chapter 2 includes instructions for authors from a peer reviewed journal aimed for publication (*Ethnicity and Disease Journal*). Chapter 3 is a general summary of the results, findings and recommendations for future studies in this field. At the end of each chapter is a detailed list of the relevant references used within that chapter. Style of referencing in Chapters 1 and 3 is according to the mandatory style indicated by the relevant journal for which the manuscript is intended for publication.

* Manuscript (Chapter 2): Journal for submission – *Ethnicity and Disease.*

OUTLINE OF STUDY

The outline of this study is as follows:

- Chapter 1: General introduction, literature overview, research question, aim, hypothesis.
- Chapter 2: Cardiovascular function and psychological distress in urbanized black South Africans: The SABPA study.
- Chapter 3: Introduction, summary and main findings, discussion of main findings, comparison with relevant literature, chance and confounding, weakness of study, final conclusion, recommendations.
- Addendums: General Health Questionnaire (GHQ-28) and Patient Health Questionnaire (PHQ-9).

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LIST OF ABBREVIATIONS

BP	-Blood Pressure
DBP	-Diastolic Blood Pressure
SBP	-Systolic Blood Pressure
PWV	-Pulse Wave Velocity
MAP	-Mean Arterial Pressure
C_w	-Arterial ('Windkessel') compliance
BMI	-Body Mass Index
HR	-Heart Rate
HRV	- Heart Rate Variability
SD	-Standard Deviation
LVH	-Left Ventricular Hypertrophy
CVD	-Cardiovascular Diseases
GHQ-28	-28-item version of the General Health Questionnaire
PHQ-9	-9-item version of the Patient Health Questionnaire
HPA	-Hypothalamic-Pituitary-Adrenal system
ANCOVA	- Analysis of Covariance
WHO	-World Health Organization
SAM	-Sympathetic-Adrenal-Medullary system

GAS	-General Adaptation Syndrome
DSM-IV	-Diagnostic and Statistical Manual of Mental Disorders
ACTH	-Corticotrophin
CRF	-Corticotrophin Releasing Factor
SNS	-Sympathetic Nervous System
SA	-Sympathoadrenal
SABPA	-Sympathetic Activity and Ambulatory Blood Pressure in Africans
CHD	-Coronary Heart Disease
GHQ-SS	-General Health Questionnaire: Somatic Symptoms
GHQ-AS	-General Health Questionnaire: Anxiety Symptoms
GHQ-SD	-General Health Questionnaire: Social Dysfunction
GHQ-DS	-General Health Questionnaire: Depression Symptoms
HT	-Hypertension / Hypertensive
NT	-Normotention / Normotensive

CHAPTER 1

INTRODUCTION AND LITERATURE STUDY

General Introduction

Cardiovascular disease (CVD) is one of the leading causes of death worldwide, with the greatest mortality rates occurring in low and middle income countries. [1] CVD is often termed as multi-factorial, as it can be caused by a combination of interwoven factors such as hypertension, diabetes, obesity, smoking, alcohol consumption and physical inactivity.[2,3] According to Benjamin *et al.*, [2] the burden of risk factors in a specified geographical region closely correlates with the prevalence patterns of that disease in that given area. With this in mind it is clear that there has been an increase in the prevalence of risk factors such as hypertension, obesity and diabetes in Sub-Saharan Africa and accordingly, an increase in the prevalence of CVD.[4,5,6] It still remains largely unclear whether stress and more specifically the experience of psychological distress may contribute to this observed increase in the prevalence in CVD in these populations.

There are many different definitions of what stress is, depending whether the term is used by psychologists, medical professionals, management consultants or others. In general the term refers to the perceptions and responses of humans trying to adapt to the challenges of everyday life.[7] The most commonly accepted definition is that stress is a condition or feeling experienced when a person perceives that emotional and physical demands exceed the personal and social resources the individual is able to mobilise.[8,9,10] Stress may be experienced either positively or negatively, depending on a number of factors. The term "eustress" refers to an adaptive response promoting the activation of internal resources to meet emotional and environmental demands and achieve goals. [11]

Psychological distress, on the other hand, occurs when the demands of a situation exceed the individual's adaptive resources and the person can, therefore, not adapt or cope with persistent stress.[12, 13] Psychological distress is a concept that is often embedded and discussed in the context of strain, stress and distress and is seldom defined as a distinct concept.[14] In this study, however, the term psychological distress will be used to refer to persistent stress that is not resolved through coping or adaptation. With increasing environmental demands this inability to adapt or cope may manifest as behavioural (e.g. absenteeism, accident proneness and drug abuse), psychological (e.g. depression, burnout and psychosomatic complaints) and medical (heart disease and other physical illnesses) consequences.[13, 15, 16, 17] In this study psychological stress will be operationalised through a number of the so-called psychological consequences or outcomes of long-term exposure to stress to which an individual is unable to adapt. These outcomes, which include individual's self-reported experience of anxiety, social dysfunction, somatic complaints and depression, will be taken as representative of the level of psychological distress that an individual has been experiencing.

One of the environmental demands that has recently received increased research attention as a source of psychological distress in an African context is urbanisation.[17, 18, 19] With rapid urbanisation, the loss of social and cultural support may lead to psychosocial disruption and one of the main psychological consequences of distress namely depression sets in.[17] The WHO defines depression as a common mental disorder that presents as a depressed mood, lack of interest, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy and poor concentration. When these problems become chronic it

may lead to substantial impairments in an individual's ability to take care of his or her everyday responsibilities.[20] In addition to the onset of depression researchers have found that urbanisation may result in an elevation in vascular reactivity in Africans.[17, 19, 21]

Depression has become a major interest in psychosomatic research as one of the psychological outcomes of distress. Physiologically depression may affect the cardiovascular system through direct and indirect mechanisms. Direct mechanisms include the nervous system activation, systemic and localized inflammation, cardiac rhythm disturbances and hypercoagulability which negatively influence the cardiovascular system.[22] Indirectly, depression may affect the cardiovascular system through behavioural adaptation to unhealthy lifestyle changes such as an increase in alcohol and tobacco consumption, physical inactivity and high fatty acid intake, all of which are cardiovascular risk factors.[23]

Studies in the past have shown a relationship between depression and CVD such as coronary heart disease and coronary artery disease.[23, 24]Unfortunately these studies focused on depression and CVD post-cardiac event. Conflicting results were found with regards to depression and the development of hypertension in the African-American population. Shinn *et al.*[25] found that their results did not support the role of depressive symptoms in the development of hypertension in normotensive adults.[25] Other researchers, on the other hand, found that the association between depression and the risk of hypertension compares favourably with better established predictors of hypertension such as obesity.[26] To our knowledge investigations exploring these aspects have not been done in the African context. Thus, more research on the relationship between depression

as an outcome of psychological distress and cardiovascular dysfunction in an African context may be warranted.

The aim of this study was, therefore, to investigate whether there is a relationship between psychological distress, as operationalised through the self-reported experience of anxiety, social dysfunction, somatic complaints, depression and cardiovascular dysfunction in urbanised black Africans of the North West Province.

STRESS

Defining stress

Stress is a concept that has been developed over the past decades from Selye's physiological definition, which is widely accepted as a definition in research, to a more cognitive approach focusing on the relationship between the individual and the environment.[7,27] Irrespective of the definition used, fundamentally stress is a condition or feeling experienced when a person perceives that emotional and physical demands exceed the personal and social resources the individual is able to mobilise and this is linked to the onset of distress and disorders.[8, 9, 10, 28,29]

THE STRESS RESPONSE

The stress response begins with a stressor, the perceived threat, or stimulus that causes some form of effect on the organism instigating the onset of human stress response process within an individual.[7, 30] Stressors may differ in duration and intensity. *Chronic stressors* are persistent events or stimuli that an individual is exposed to on an unchanging continuous basis.[31, 32] These stressors are constant in nature but may vary in intensity. *Acute stressors* are events or stimuli of a short duration and high intensity which have a specified time of onset.[31, 32, 33] Traumatic life events such as environmental disasters and sudden death of a family member are examples of acute stressors.[32]

It is evident from the literature that individuals experience events differently. An event that may be classified as a chronic stressor to one individual may be experienced as part of daily life for another.[32] Thus perceptions or appraisals of the events, situations or stimuli are important elements in the determination of one's safety in relation to one's environment.[27] Lazarus [27] described two types of appraisals, *primary* and *secondary appraisal*. *Primary appraisal* is influenced by individual characteristics and environmental factors. This type of appraisal involves the interpretation of how stressful the potential problem may be. *Secondary appraisal* involves the evaluation of whether an individual's coping resources are adequate to deal with the potential stressor when the situation is deemed as stressful.[27, 28] Secondary appraisal occurs in relation (and not necessarily after) to the primary appraisal of a situation, in other words the evaluation is dependent on the subjective interpretation of whether an event or situation poses a threat

to the individuals well-being. Therefore, secondary appraisal can be influenced by a number of factors such as demands, constraints and opportunities resulting in the generation of emotions attributed to a particular event or situation.[27,28]

According to Selye, stress may be experienced positively (eustress) or negatively (distress) depending on a number of factors. As previously mentioned the term "eustress" refers to an adaptive response promoting the activation of internal resources to meet emotional and environmental demands and achieve goals.[11] Selye considered the relation between eustress and distress fundamental in the attainment of a greater a well-being.[30] When the experience of stress reaches a threshold level (which may be different for each individual), any additional stress, situation or event can promote the onset of distress which is characterised by behavioural and physiological responses that can lead to disorder or disease.[7,30] It is thus clear from Selye's theory of stress that stress can be experienced in a beneficial or in a harmful way.

In addition to these early designations, McEwen [34] formulated two new terms to describe the body's responses to stress, 'allostasis' and 'allostatic load'. 'Allostasis' literally means maintaining stability through change and the term 'allostatic load' refers to the wear and tear the body experiences due to repeated cycles of allostasis. When the brain perceives any situation as stressful, physiological and behavioural responses are initiated leading to allostasis and adaptation according to McEwen.[34] Persistent stress results in repeated cycles of allostasis and the accumulation of allostatic load. During persistent environmental demands stress may manifest as diverse behavioural (e.g. poor diet and

substance abuse), psychological (e.g. depression and psychosomatic complaints) and medical symptoms (e.g. cardiovascular dysfunction and physical illnesses).[34,35]

It is clear from the above-mentioned models that the experience of stress, whether mental or physical, over time can be cumulative and detrimental. A stressful event becomes detrimental when the individual fails to adapt or cope with the persistent stress. This may manifest as behavioural, psychological and medical symptoms that are harmful to the individual and are linked to the onset of distress and cardiovascular disorders.

DISTRESS

'Distress' is a term first used by Selye to describe the negative experience of stress and the failure to resolve persistent stress through coping or adaptation.[11] Psychological distress occurs when the demands of a situation exceed the individual's adaptive resources and the person can, therefore, not adapt or cope with persistent stress.[12,13] The concept of psychological distress is often embedded in the context of strain, stress and distress and is seldom defined as a distinct concept.[14] Ambiguity exists in the literature in terms of the context in which stress and distress are used. In this study the term 'psychological distress' refers to persistent stress that is not resolved through adaptation.

Outcomes of psychological distress

As an outcome of psychological distress, depression is a psychiatric condition that has received attention in most lines of research.[36] Depression is a common mental disorder that is characterised by depressed mood, sadness, loss of interest and pleasure, poor concentration, decreased energy, feelings of guilt and low self-worth and disturbance in sleeping and eating patterns.[20, 37] The extent, severity and duration of the depressive symptoms can help differentiate between depression from normal mood changes.[20] A clear distinction can be made between chronic depressive symptoms which result from persistent depressed mood over a period of months or years and acute symptoms occurring in response to everyday life events.[37]

Other outcomes of psychological distress include the experience of anxiety and insomnia, social dysfunction and somatic symptoms.[38] A variety of psychological instruments have been developed and implemented in measuring psychological distress and its outcomes.[38]

Measuring psychological distress

Psychological distress and its consequences can be measured by making use a variety of psychological instruments.[39] The ones that will be utilised in this study are the General Health Questionnaire and the Patient Health Questionnaire.[40, 41]

1. The General Health Questionnaire (GHQ)[38]

The General Health Questionnaire (GHQ-28) is a self-report questionnaire that assesses psychological well-being by detecting those likely to have or are at risk for developing

psychiatric disorders.[38, 39, 40] The questionnaire is useful in the understanding of various sources of distress in occupational research.[39]

The questionnaire consists of four (4) subscales that measure the common mental health symptoms/domains of depression, anxiety, somatic symptoms and social withdrawal.[39]

1.1 Somatic Symptoms

Perceived stress is associated with decreased psychological well-being and increased somatic symptoms.[42, 43] Somatic manifestations of depression occur across all cultures and have been variously described as functional, medically unexplained somatic symptoms, somatic preoccupation or worry about illness, or undue emphasis on the somatic manifestations of psychiatric disorders.[44, 45] In African-Americans, severity of somatic symptoms was found to be higher than in the Caucasian group.[46] In an African context, somatic symptoms in depression are extremely common features.[44] Somatic depressive symptoms are associated with poor health status and predicted cardiovascular mortality and cardiac mortality.[47]

1.2 Anxiety

Anxiety is one of the most common symptoms of psychological distress and is associated with a variety of somatic symptom patterns. Varied anxiety states have been linked to autonomic nervous system activity such as rapid heart rate, shortness of breath and sweating.[48] These symptoms are frequently viewed as signs of increased sympathetic activity.[48] Long-term sympathetic activation has been associated with cardiovascular

dysfunction. Both depression and anxiety have been shown to be associated with increased risk for cardiovascular diseases such as CAD.[49]

1.3 Social dysfunction

Substantial amounts of literature from epidemiological, sociological and health psychology research have demonstrated the association between social support and morbidity and mortality risks.[50] Social dysfunction is an indication of the disintegration of a person's social support network and the loss of both given and received support.[51] As the importance of the social support network is an important characteristic of collectivistic cultures, the lack of social support may result in psychosocial dysfunction and the onset of depression.[17] Social support is increasingly being recognised as a predictor of CHD etiology and prognosis.[52] In Africans the loss in social support resulting from rapid urbanisation is associated with increased vascular reactivity.[6, 17, 18]

1.4 Symptoms of Depression

Depressive symptoms, that result from chronic exposure to stress over a substantial period of time, have deleterious effects on cardiovascular functioning.[53] Symptoms of depression have been related to future incidences of hypertension.[54] In addition to the etiological link to heart disease, depression may be a risk factor for mortality following a cardiac event.[53, 55] Symptoms of depression appear to be related to exaggerated heart rate (HR), blood pressure (BP) and vascular resistance response.[56]

Items

Multiple versions of the GHQ are available using 12, 28, 30, 60 items, but the 28-item version is used most widely.[39]

An example of items used in this questionnaire include 'Have you found everything getting on top of you'; 'Have you been getting scared or panicking for no reason?' and 'Have you been getting edgy and bad tempered'. Each of the above are then accompanied by 4 possible responses; 'not at all', 'no more than usual', 'rather more then usual' and 'much more than usual'. The GHQ may be evaluated in a variety of ways. In this study each item was evaluated using the binary scoring method.[57] The two least symptomatic answers are given a score of nil (0) whilst the two most symptomatic answers are given value of one (1). Total scores exceeding the threshold of 4 are classified as achieving 'psychiatric caseness'. In general practice, individuals classified as achieving 'psychiatry caseness' would be likely to receive further attention.[39]

Validity

The reliability coefficients reported in various studies ranged from 0.78 to 0.95. Wissing and Van Eeden [58] reported a reliability coefficient of 0.91 in a South African sample. An acceptable reliability and validity indices for use in the Setswana-speaking group has also been shown.[59]

2. Patient Health Questionnaire (PHQ) [41]

The Patient Health Questionnaire (PHQ) is a 9-item instrument for making criteria-based diagnoses of depressive disorders and it is also a reliable and valid measure of depression

severity. [41] Being half the length of other depression measurements, the PHQ-9 is ideal as it has both sensitivity and reliability. The scale is based on the actual 9 criteria of diagnosis of the DSM-IV depressive disorders. The PHQ assesses 8 diagnoses divided into threshold disorders (disorders that correspond to specific DSM-IV diagnoses i.e. major depressive disorder) and sub-threshold disorders (disorders whose criteria include fewer symptoms than required for any specific DSM-IV diagnoses i.e. other depressive *disorders*). The questionnaire scores each of the nine (9) DSM-IV criteria as "0" (not at all) to "3" (nearly every day). For analysis the PHQ-9 scores are divided into the following categories of increasing severity: 0-4, 5-9, 10-14, 15-19 and 20 or greater which represent minimal, mild, moderate, moderately severe, and severe depression respectively. Scores less then five (5) signify the absence of depressive disorders; scores of 5-9 predominately represent no depression or sub-threshold depression; scores of 10-14 represent a spectrum of individuals who may or may not display depression. Scores of 15 or higher usually are indicative of major depression.[41]

Items

At 9 items, the PHQ-9 has comparable sensitivity and specificity to many other larger depression measures. The PHQ-9 is based directly on the diagnostic criteria for major depressive disorder in the Diagnostic and Statistical Manual Fourth Edition (DSM-IV). There are two components of the PHQ-9; assessing symptoms and functional impairment to make a tentative depression diagnosis, and deriving a severity score to help select and monitor treatment.[41]

Validity

Both construct and criterion validity have been established in primary health care settings rendering the PHQ-9 a reliable and valid measure of depression in this sample. The combination of brevity, construct and criterion validity makes the PHQ-9 a useful, dual-purpose diagnostic tool for assessing severity of depressive disorders. [41]

Physiological outcomes of distress: The General Adaptation Syndrome

Failure to adapt or cope with persistent stress may generate continual physiological stimulation characterised by incessant activation of two primary systems associated with the physiological stress response, the sympathetic-adrenal-medullary system (SAM) and the hypothalamic-pituitary-adrenocortical (HPA), that can produce a cascade of negative pathological consequences.[60] The resultant dysregulation of these systems may lead to high catecholamine levels, autonomic dysfunction and other peripheral effects such as increased peripheral resistance .[10, 22, 60-62]

Selye[7] researched the physiological outcomes of stress and characterised them into a three (3) stage response model known as the general adaptation syndrome (GAS). According to GAS, the stress response may be broken into 3 stages, namely alarm (stage 1), resistance (stage 2) and finally, exhaustion (stage 3). The identification or realisation of a threat results in a state of alarm and this leads to a production of epinephrine in order to elicit a fight or flight response. Included in this stage is the activation of the HPA axis, thus leading to the production of cortisol.[63] Persistence of the stress results in the activation of various physiological coping mechanisms (stage 2). The body tries to adapt

to the strains or demands of the environment, but the body cannot keep up with this indefinitely. Depletion of the body's recourses (stage 3) and the inability to maintain normal function will lead to the reappearance of the initial autonomic nervous system (ANS) symptoms. Extensions of this stage will lead to long-term damage, thus resulting in illnesses such as depression and cardiovascular dysfunction.[7]

Chronic activation of the SNS and HPA will result in an elevated secretion of catecholamines and other vasoactive substances such as angiotensin II and ACTH.[63] Elevated plasma levels of catecholamines may lead to Na^+ retention and volume overload [64] whilst vasoactive substances will contribute to increased vascular resistance.[63] Both volume overload and exaggerated vascular resistance will contribute to an elevation in BP and future incidences of hypertension.[65,66] This persistent elevation of BP will result in pressure overload and the sustained pressure and volume overload will progressively lead to morphological changes in left ventricular geometry and subsequently to an increase in ventricular mass.[67] In a population in transition, chronic exposure to stress will lead to an increase in sympathetic reactivity and an elevated normal BP. [6,17-19,21] Repeat exposures to this wear and tear may be detrimental (pressure and volume overload) to vascular health (morphological changes in arterial vasculature), subsequently leading to the increase in ventricular mass and development of left ventricular hypertrophy.[34, 35, 65] The physiological response of the body to persistent stress by making use of Selye's General adaptation syndrome model, is briefly described in Figure 1.[7]

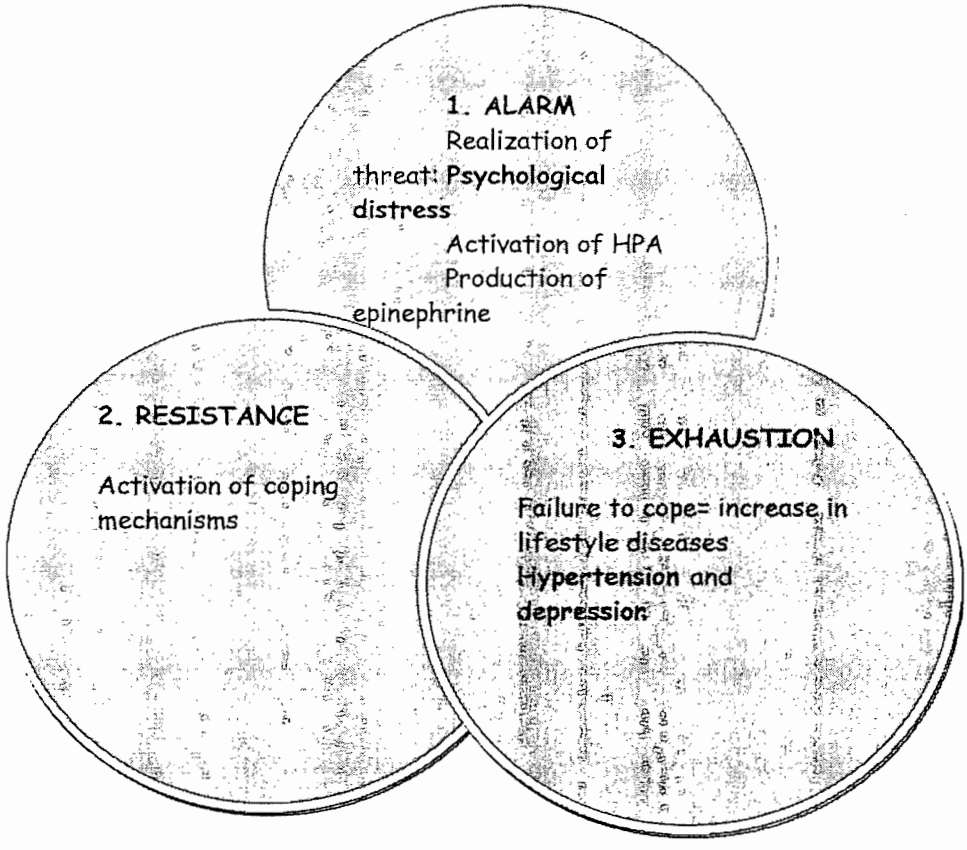

Figure 1.A brief description of Hans Selyes General Adaptation Syndrome.[7]

Urbanisation, Distress and Hypertension

With rapid urbanisation, the loss of social and cultural support may lead to psychosocial disruption and psychological distress may set in.[17]As a source of psychological distress, urbanisation is an environmental demand that has received increased research attention in an African context in the past decade.[17, 18, 19] The process of rapid urbanisation has led to

social and cultural disruption leading to increased levels of stress.[17] Urbanisation has also been associated with a significant increase in lifestyle-related diseases such as hypertension, coronary heart disease, diabetes and cerebrovascular disease.[19] Epidemiological studies have established that the prevalence of hypertension is increasing in the African population [6, 17-19,21,25] The causative factors for hypertension in the African population may vary from abnormalities in the renin-angiotensin-aldosterone system, putative role of the sodium channel and environmental influences.[5] Increased salt sensitivity and low rennin activity have been identified as important contributors to hypertension in Africans.[68, 69] Therefore, these genetic factors further predispose Africans to an exaggerated vascular reactivity in response to environmental stressors compared to other ethnic groups.

Environmental stressors, such as those brought about by urbanisation, are likely to enhance sympathetic activity and contribute to the early development and severe progression of hypertension in blacks.[65, 66] Malan [6] and colleagues found an association between stress experienced during urbanisation and an increase in BP and high prevalence of hypertension.[6, 17] Figure 2 is a simplified schematic presentation that describes the process by which chronic exposure to environmental stressors contributes to the development and progression of hypertension.

There is ample evidence that sympathetic hyperactivity is a characteristic feature of some forms of hypertension, especially in the early stages of essential hypertension. [64-66] Studies done on HT have shown that subjects with hypertension exhibit excessive cardiovascular risk factors like left ventricular and arteriolar hypertrophy.[67] In addition to

a raise in BP, adrenergic stimulation may induce target end organ damage by both hemodynamic and non hemodynamic mechanisms.[69] Adrenergic stimulation has been associated with left ventricular hypertrophy as well as vascular hypertrophy and stiffening.[70] As the hypertensive state escalates, hemodynamic pattern changes from a high cardiac output mediated by the stimulation of β_1-adrenergic pathways to a high vascular resistance pattern mediated by α-adrenergic pathways.[5, 17, 18] The maintenance of BP shifts from the central mechanisms to the vascular mechanisms which promote an increase in vascular resistance that lead to hypertension-related morbidity and mortality.[17, 67, 70] An α-adrenergic vascular reactivity has been found in Africans. This resulted in higher vasoconstriction and decreased vascular compliance.[5, 64]

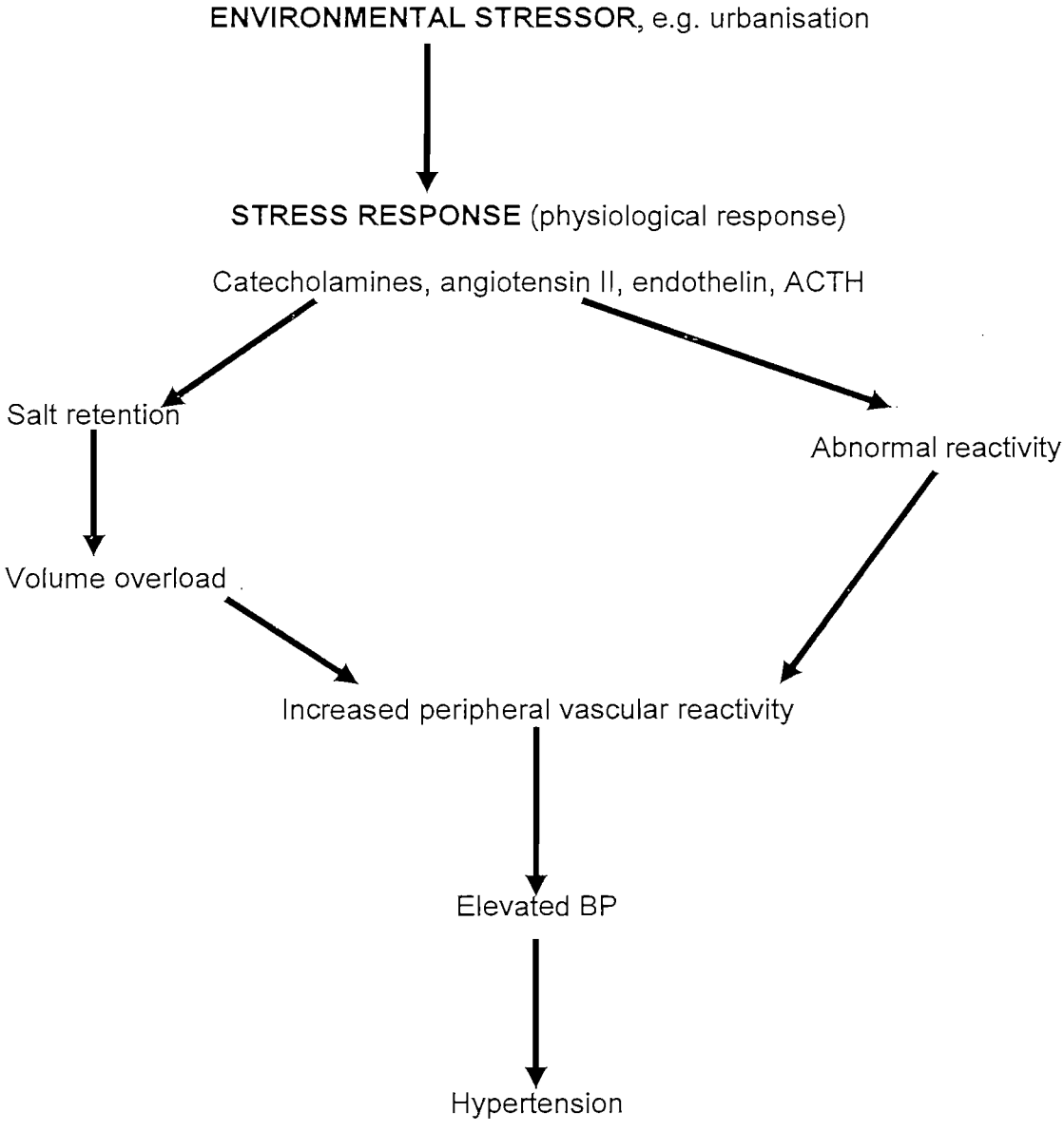

Figure 2.Schematic representation of the interaction between environmental stressors and the development of hypertension in Africans.[66]

Distress, Depression and Cardiovascular disease

The presence of psychological distress has been associated with incidences of CVD in several prospective cohort studies. In Caucasian subjects with high levels of distress, it was found that distress was a predictor of all-cause mortality in that population group.[71] In a follow-up multicultural study in African-American subjects their experience of psychological distress was associated with a higher mortality rate in comparison to other ethnic groups.[72] Studies done on the African population have provided an association between psychological distress experienced from urbanisation, and the prevalence of hypertension.[6, 17, 18, 19] Limited literature exist on distress and CVD in the African population. Although ample literature exist linking psychological distress and CVD risk, the intermediate mechanisms are yet to be fully elucidated in the African population. Behavioural mechanisms such as smoking, alcohol consumption and physical inactivity maybe an adaptation or coping response to psychological distress, and may thus be an important intermediate factor in the disease processes.[60, 62, 67, 70]

Psychological distress may lead to CVD via several different mechanisms. Firstly, it maybe indirectly associated with CVD through its associations with adoption of unhealthy behaviours such as excessive alcohol consumption, physical inactivity and eating fatty foods which are also well known risk factors for CVD.[73,74] Secondly, psychological distress maybe a product of exposure to situations of low perceived control.[73] It is well documented in the literature that Africans experience elevated vascular reactivity in response to environmental stressors.[6, 17, 65, 66] For instance, Van Rooyen [65] and colleagues found that children who were exposed to a violent environment

had higher vascular activity compared to those exposed to situations of low violence.[65]

Finally, psychological distress may lead to unhealthy coping behaviour that especially in the context of low perceived control may indirectly lead to increased CVD risk. Malan *et al.*[17] for example noted that Africans with active coping styles had an exaggerated vascular reactivity compared to individuals who have adapted to a more passive coping style, therefore, it seems that Africans who felt they had some control over their situation (AC) experienced exaggerated vascular reactivity compared to those who have low perceived control. Behaviourally they cope better but physiologically the cost of coping leads to more adverse CV responses and HT.[17]

Psychological distress primarily activates the sympathetic or hypothalamic pituitary-adrenal axis systems which trigger pathophysiological mechanisms that include inflammation, haemostasis and altered metabolic and cardiac autonomic control.[23] For example, Africans who are exposed to high levels of environmental stress have been found to exhibit heightened sympathetic activity.[21] This enhanced sympathetic activity may contribute to the early development and severe progression of hypertension in Africans, which in itself is a CVD risk factor in this population .[66]

As an outcome of long-term exposure to psychological distress, depression has received ample attention in most lines of clinical research. It is estimated that at any given time 5-10% of the population suffer from depression.[20] In the African context, the prevalence of depression has not been recorded. With the use of the Mental Health Continuum, which is a mental well-being measure, an estimated prevalence of individuals with low levels of psychological well-being (languishing) in the African population can be deduced as these

individuals who are more likely to suffer from psychiatry disorders like depression.[75] In a study done by Van Rooy [75] *et al.*, 6% of their subjects were languishing and these subjects had low levels of emotional, social and psychological well-being, and may represent individuals who are at high risk of developing psychiatric disorders such as depression.[75]

Depression has been associated with the hyperactivity of the HPA system and the sympathetic nervous system (SNS). Both these systems result in the release of glucocorticoids and catecholamines respectively.[10] These two systems are interconnected, the activation of one of these systems influences changes in the other. The HPA system augments the sympthoadrenal system via central regulatory pathways and the development of CVD. [22] The heightened levels of glucocorticoids, particularly cortisol, have a number of effects on the physiological system. The resulting increase in plasma catecholamine leads to vasoconstriction, platelet activation and elevated heart rate (HR).[10, 22] Researchers have found that in addition to the elevated circulating plasma levels of epinephrine, depressed patients manifest elevated resting HR and decreased HRV compared to non-depressed controls.[61] According to Carney *et al.*,[61] these conditions are a result of autonomic dysregulation (reduction in parasympathetic activity and an increase in sympathetic activity) that have been associated with sudden cardiac death in patients with CHD.[66] Additionally, elevated catecholamine levels may promote pro-thrombotic processes by potentiating platelet activation and increasing hemodynamic stress on vascular walls, or by inhibiting vascular eicosanoid synthesis.[76, 77] The cost of the increased hemodynamic stress is changes in structural and functional properties of the large arteries and an increase in LV mass. Increased levels of coagulating-promoting

factors have been shown to predict coronary syndromes such as myocardial infarctions (MI) and sudden cardiac death in healthy individuals and in patients with CVD.[78]

SUMMARY

Figure 3 summarises the main ideas discussed so far. Persistent stress elicits both behavioural and physiological responses. It is clear from the figure that if a stressor is perceived negatively, both behavioural and physiological mechanisms are initiated resulting in the increased risk for both physical and psychiatric disease.

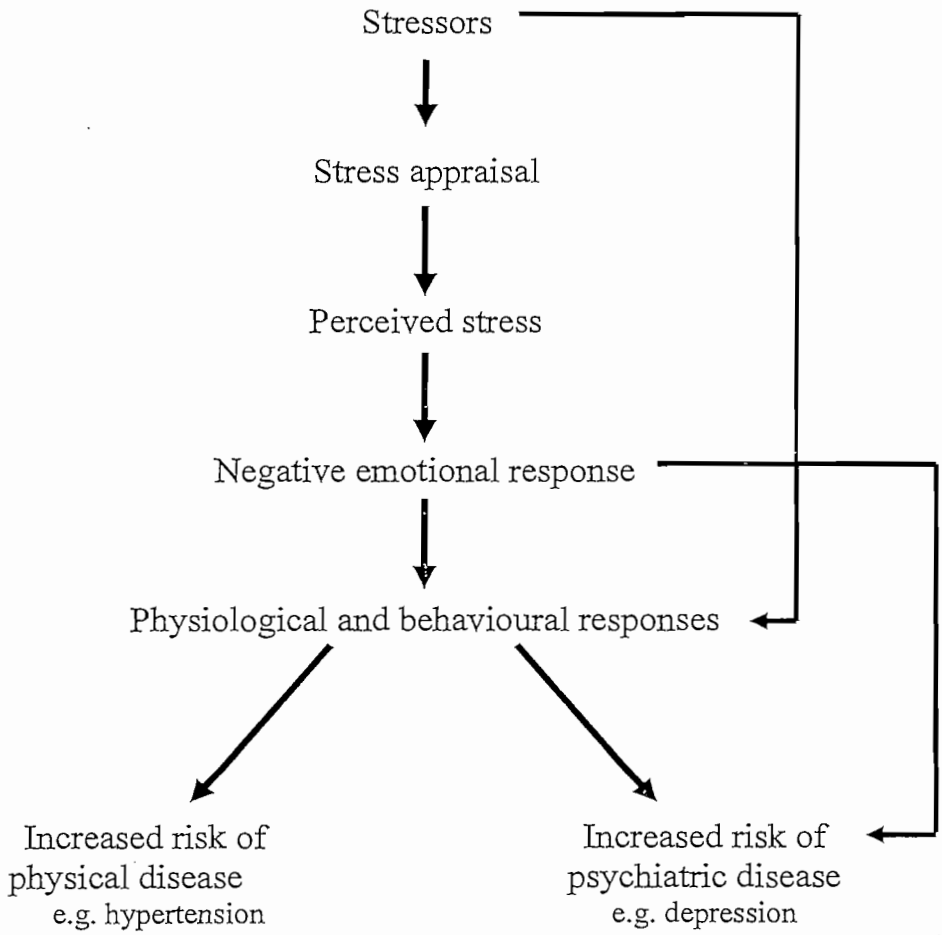

Figure 3.Physiological and behavioral response to environmental stressors and their subsequent consequences in the development of pathological conditions.

RESEARCH QUESTION

Although a number of studies have investigated depression and the pathology of CVD, only a limited number focuses on psychological distress and cardiovascular function pre-hypertension. From that limited percentage, none focused on depression and cardiovascular function in Africans. Therefore, an investigation focusing on psychological distress and cardiovascular function in the African population is warranted.

AIM

The aim of this study was, therefore, to investigate whether there is a relationship between psychological distress and the development of cardiovascular dysfunction in urbanised black Africans of the North West Province.

HYPOTHESIS

1. There is a relationship between perception of poorer health (GHQ) and cardiovascular dysfunction in Africans
2. An association exists between depression, perception of health, hypertension and cardiovascular function in Africans.

REFERENCES:

1. WHO (World Health Organization). Cardiovascular disease: prevention and control. Available at: http://www.who.int/mediacentre/factsheets/fs317/en/index.html. Accessed November 7, 2008.
2. Benjamin EJ, Smith SC, Cooper RS *et al.* Task Force #1—magnitude of the prevention problem: opportunities and challenges. *J Am Coll Cardiol,* 2002; 40:588-603.
3. Reddy KS, Yusuf S. Emerging epidemic of cardiovascular disease in developing countries. *Circulation.*1998; 97:596-601.
4. SADHS: Department of Health, Medical Research Council & Measure DHS+. South Africa Demographic and Health Survey 1998, Available at: http://www.hst.org.za/indicators/SADHS_1998_Full.pdf . Accessed November 2, 2008.
5. Opie LH, Seedat YK. Hypertension in Sub-Saharan African populations. *Circulation.* 2005; 112:3562-3568.
6. Malan L, Malan NT, Wissing MP *et al.*, Coping with urbanisation: A cardiometabolic risk? *Biol Psychol.* 2008; 323-328.
7. Selyes H. *The Stress of life.* New York: McGraw-Hill; 1956.
8. McEwen BS. Stress, adaptation, and disease: Allostasis and allostatic load. *Ann N Y Acad Sci.*1998; 840: 33-44.
9. Lazarus RS. From psychological stress to the emotions: A history of changing outlooks. *Annu Rev Psychol.* 1993; 44: 1-21.

10. Vale S. Psychological stress and cardiovascular diseases. *J Postgrad Med.* 2005; 81: 429-435.

11. Selye H. Confusion and controversy in the stress field. *J Hum Stress.* 1975; 1:37-44.

12. Folkman S, Lazarus RS, Dunkel-Schetter C *et al.*, Dynamics of stressful encounter, cognitive appraisal, and coping and encounter outcomes. *Journal of personality and Social psychology.*1986;50(5):992-1003.

13. De Kloet RE, Joels M, Holsboer F. Stress and the brain: from adaptation to disease. *Nat Rev Neurosci.* 2005; 6(6):463-475.

14. Ridner SH. Psychological distress: concept analysis. *J Advan Nurs.* 2004; 45(5): 536-545.

15. Quick JC, Quick JD, Nelson DL *et al.*, *Preventative stress management in organizations.* Washington DC: American Psychology Association; 1997.

16. Voster HH, Wissing MP, Venter CS *et al.*, The impact of urbanization on physical and mental health of Africans in the North-West Province of South Africa: The THUSA study. *S Afr J Sci.* 2000; 96: 505-514.

17. Malan L, Schutte AE, Malan NT *et al*, Coping mechanisms, perception of health and cardiovascular dysfunction in Africans. *Int J Psychophysiol.* 2006; 61:158-166.

18. Van Rooyen JM, Kruger HS, Huisman HH *et al.*, An epidemiological study of hypertension and its determinants in a population in transition: the THUSA study. *J Hum.* Hypertens. 2000; 14:779-787.

19. Malan NT, Van De Merwe JS, Huisman HW *et al.*, A comparison of cardiovascular reactivity of rural blacks, urban blacks and whites. *Stress Med.* 1992; 8:241-246.

20. WHO (World Health Organization). Depression. Available at: http://www.who.int/mental_health/management/depression/definition/enAccessed November 7, 2008.

21. Van Rooyen JM, Nienaber AW, Huisman HW *et al.*, Differences in resting cardiovascular parameters in 10-to-15 year old children of different ethnicity: the contribution of physiological and psychological factors. *Ann Behav Med.* 2004; 28(3)163-170.

22. Joynt KE, Whellan DJ, O'Connor CM. Depression and cardiovascular disease: mechanisms of interaction. *Biol Psychiatry.* 2003; 54(3): 248-261.

23. Stansfeld SA, Fuhrer R, Shipley MJ *et al.*, Psychological distress a risk factor for coronary heart disease in the Whitehall II Study. *Int J Epidemiol.* 2002; 31:248-255.

24. Lett HS, Blumenthal JA, Babyak MA *et al.*, Depression as a Risk factor for coronary artery disease: Evidence, mechanisms, and treatment. *Psychosom Med.* 2004; 66:305-315.

25. Shinn EH, Poston WSC, Kimball KT *et al.*, Blood pressure and symptoms of depression and anxiety: a prospective study. *Am J Hypertens.* 2001; 14:660-664.

26. Kabir AA, Whelton PK, Khan MM *et al.*, Association of symptoms of depression and Obesity with hypertension: the Bogalusa Heart study. *Am J Hypertens.* 2005; 19(6):639-645.

27. Lazarus R.S. *Stress and emotion: New synthesis*. San Francisco: Springer Publishing Company; 1999.

28. Carver CS, Scheier MF, Weintraub JK. Assessing coping strategies: theoretically base approach. *J Pers Soc Psychol*.1989; 57:267-283.

29. Matthieu MM, Ivanoff A. Using stress, appraisal, and coping theories in clinical practice: Assessments of coping strategies after disasters. *Brief Treat Crisis Interven.* 2006; 6(4):337-348.

30. Everly GS, Lating JM. *A clinical guide to the treatment of the human stress response*. New York: Kluwer Academic; 2002.

31. Day AL, Livingstone HA. Chronic and acute stressors amongst military personal: do coping styles buffer their negative impact on health? *J Occup Health Psychol.* 2001; 6:348-360.

32. Hahn SE, Smith CS. Daily hassels and chronic stressors: conceptual and measurement issues. *Stress Med.*1999;15(2):89-101.

33. Dimsdale JE. Psychological stress and cardiovascular function. *J Am Coll Cardiol.* 2008; 51(13):1237-1246.

34. Stewart A. The detrimental effects of allostasis: Allostatic load as a measure of cumulative stress. *J Physiol Anthropol.* 2006; 25(1): 133-145.

35. McEwen BS, Seeman T. Protective and damaging effects of mediators of stress-Elaborating and testing the concepts of allostasis and allostatic load. In Alder NE, Marmot M, McEwen BS, Stewart J eds. *Socioeconomic Status and Health in industrialised nations*. New York Academy of Science, New York,.1999:30-47.

36. Carney RM, Freedland KE, Miller GE *et al.,* Depression as a risk factor for cardiac mortality and morbidity: a review of potential mechanisms. *J Psychosom Res.* 2002; 53: 897–902.

37. Hamer M, Tanaka G, Okamura H *et al.*, The effects of depressive symptoms on cardiovascular and catecholamine responses to induction of depressive mood. *Biol Psychol.* 2007; 74(1):20-25.

38. Goldberg DP, Hiller VF. A scaled version of the General health Questionnaire. *Psychol Med.* 1979; 9: 139-145.

39. Jackson G. The General Health Questionnaire. *Occup Med.* 2007; 57(1):79.

40. Goldberg DP, Hiller. *Manual of General Health Questionnaire.* England NFER Publishing; 1978.

41. Kroenke K, Spitzer RL, Williams. The PHQ-9: Validity of a brief depression Severity Measure. *J Gen Intern Med.* 2001; 16:606-613.

42. Begley TM. Coping strategies as a predictor of employee distress and turnover after an organisation consolidation: a longitudinal analysis. *Occup Organizational Psychol.*1998; 38(5):477-500.

43. Cooper CL, Kelly M. Occupational stress in head teachers: a national UK study. *Br J Educ Psychol.* 1993; 63 (1): 130-143.

44. Okulate GT, Olayinka MO, Jones OBE *et al.*, Somatic symptoms in depression: evalution of their diagnostic weight in an African setting. *Br J Psychiatry.* 2004;184:422-427.

45. Kirmayer LJ, Robbins JM, Dworkind M *et al.*, Somatization and the recognition of depression and anxiety in primary care. *Am J Psychiatry.* 1993; 150:734-741.

46. Brown C, Schulberg HC, Madonia MJ *et al.*, Clinical presentations of major depression by African Americans and Whites in the primary medical care practice. *J Affect disord.* 1996; 41:181-191.

47. de Jonge P, Ormel J, Van den Brink RHS. Symptom dimensions of depression following myocardial infarction and their relation with somatic health status and cardiovascular prognosis. *Am J Psychiatry.*2006; 163:138-144.

48. Friedman BH, Thayer JF. Autonomic balance revisited: panic anxiety, and heart rate variability. *J Psychosom Res.* 1998; 44(1):133-151.

49. Zoeller RF. Physical activity: Depression, anxiety, physical activity and cardiovascular disease: what's the connection? *Am J lifestyle Med.* 2007;1:175.

50. Seeman TE, Singer BH, Ryff CD *et al.*, Social relationships, gender, and allostatic load across two age cohorts. *Psychosom Med.* 2002, 64:395-406.

51. Lawler KA, Piferi RL, Younger JW *et al.*, A change of heart: cardiovascular correlates of forgiveness in response to interpersonal conflict. *J Behav Med.* 2003; 26:373-393.

52. Rozanski A, Blumenthal JA, Kaplan J. Impact of psychological factors on the pathogenesis of cardiovascular disease and implications for therapy. *Circulation.* 1999; 99: 2192-2217.

53. Strik JJMH, Denollet J, Lousberg R *et al.,* Comparing symptoms of depression and anxiety as predictors of cardiac events and increased health care consumption after myocardial infarction. *J Am Coll Cardiol.*2003; 42(10):1801-1807.

54. Jonas BS, Lando JF. Negative affect as a prospective risk factor for hypertension. *Psychosom Med.* 2000; 62: 188–196.

55. Lane D, Carrol D, Lip GYH. Anxiety, depression and the prognosis after myocardial infarction: is there a causal association. *J Am Coll Cardiol.* 2003; 42(10):1808-1810.

56. Hamer M, Williams E, Vuonovirta R *et al.*, The effects of effort-reward imbalance on inflammatory and cardiovascular responses to mental stress. *Psychosom Med.* 2006; 68: 408-413.

57. Goldberg DP, Gater R, Sartorius TB *et al.,* The validity of two of the GHQ in the WHO study of mental illness in general health care. *Psychol Med.* 1997; 27:191-197.

58. Wissing MP, Van Eeden C. Empirical clarification of the nature of psychological well-being. *S Afr J Psychol.* 2002; 32(1):32-44.

59. Wissing MP, Thekiso S, Stapelberg R *et al.*, *The psychometric properties of scales measuring psychological well-being in an African group: the THUSA study*. Paper presented at the International Africa Psychology Congress. Durban, South Africa; 1999.

60. Rozanski A, Kubzansky LD. Psychologic functioning and physical health: A paradigm of flexibility. *Psychosom Med.* 2005; 67:47-53.

61. Carney RM, Freedland KE, Veith RC. Depression, the autonomic nervous system, and coronary heart disease. *Psychosom Med.* 2005; 67:29-33.

62. Lovallo W, Gerin W. Psychophysiological reactivity: mechanisms and pathways to cardiovascular disease. *Psychosom Med.* 2003; 65:36-45.

63. Light KC, Kothandapani RV, Allen MT. Enhanced vascular and catecholamine responses in women with depressive symptoms. *Int J Psychophysiol.* 1998; 28:157-166.

64. Fray JCS and Douglas JG. Pathophysiology of hypertension in blacks. Oxford University press. New York. 1993: 219-232.

65. Van Rooyen JM, Husiman HW, Eloff FC *et al.*, Cardiovascular reactivity in black South African male of different age groups: the influence of urbanisation. *Ethn & Dis.* 2002; 12(1):69-75.

66. Ergul A. Hypertension in black patients: An emerging role of the endothelin system in salt-sensitive hypertension. *Hypertension.* 2000; 36:62-67.

67. Kizer R, Arnett DK, Bella JN *et al.*, Differences in Left ventricular structure between black and white hypertensive adults. *Hypertension.* 2004; 43:1182-1188.

68. Jr Wright JT, Rahman M, Scarpa A *et al.*, Determinants of salt sensitivity in black and white normotensive and hypertensive women. *Hypertension.*2003; 42:1087.

69. Johnson RJ, Gordon KL, Suga S. Renal injury and salt sensitive hypertension after exposure to catecholamines. *Hypertension.* 1999; 34:151-159.

70. Meeus F, Kourilsky O, Guerin AP. Pathophysiology of cardiovascular disease in hemodialysis patients. *Kidney Int.* 2000; 58:140-147.

71. Robinson KL, Mcbeth J, Macfarlane G. Psychological distress and premature mortality in the general population: a prospective study. *Ann Epidemiol.* 2004; 14(7):467-472.

72. Fiscella K and Franks P. Does psychological distress contribute to racial and socioeconomic disparities in mortality? *Soc Sci Med.*1997; 45(12): 1805-1809.

73. Hamer M, Molloy G, Stamatakis E. Psychological distress as risk factor for cardiovascular events. *J Am Col Cardiol.* 2008; 52(25); 2157-2162.

74. Ruuskanen JM, Ruoppila I. Physical activity and psychological well-being among people aged 65-84 years. *Age Aging.* 1995; 24:292-296.

75. Van Rooy SG, Wissing MP, Potgieter JC *et al.*, *Validation of a scale to measure psychosocial well-being in an African context.* M.A. Dissertation- North West University, Potchefstroom campus.2007: 17-37.

76. Bosma H, Marmot MG, Hemingway H *et al.*, Low job control and the risk of coronary heart disease in the Whitehall II (prospective cohort) study. *Br Med J.* 1997; 314:558-565.

77. Anfossi G, Tovati M. Role of catecholamines in platelet function: pathophysiological and clinical significance. *Eur J Clin Invest.* 1996; 32:353-370.

78. Tousoulis D, Davies G, Stefanadis C. Inflammatory and thrombotic mechanisms in coronary atherosclerosis. *Heart.* 2003; 89:993-997.